ONLINE MEASUREMENT OF GLUCOSE IN A ROTATING WALL PERFUSED VESSEL BIOREACTOR USING AN AMPEROMETRIC GLUCOSE SENSOR

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Glucose is a necessary nutrient for mammalian cell culture. A reliable, long-term stable glucose sensor is important for continuously monitoring glucose in a bioreactor. Recently, the continuous on-line detection and monitoring technologies are attractive because those on-line sensors offer several advantages including a very low cost for the instrumentation and good precision[1]. However, on-line glucose monitoring for a long-term cell run in a bioreactor by means of an amperometric enzyme sensor raises a series of intrinsic difficulties including (1) sensor sterilization (2) enzyme activity loss due to the enzyme membrane sterilization (3) locally low concentration of oxygen and (4) protein adhesion and binding on sensor membrane[2,3].

Recently, in co-operation with Markwell Medicals, we have developed and evaluated a reliable, long-term stable glucose sensor for continuously monitoring glucose in the perfused media in a rotating wall perfused vessel (RWPV) bioreactor, where BHK-21 cells were grown.

The glucose sensor, based on a hydrogen peroxide measurement, was constructed using three electrodes (two platinum and one silver/silver chloride), one enzyme membrane and a homemade flow cell. The sensor was spliced into the RWPV bioreactor system and was employed to continuously measure the glucose concentration of GTSF-2 medium on line for 30 days. The output of the sensor was converted to the glucose concentration utilizing the two-point calibration method. The steady-state response time was less than 20 minutes. The glucose concentrations as measured by the glucose sensor were compared with the glucose concentrations measured by a Beckman Glucose Analyzer. The developmental sensor was able to measure glucose accurately for 16 days using a single calibration (Figure 1).

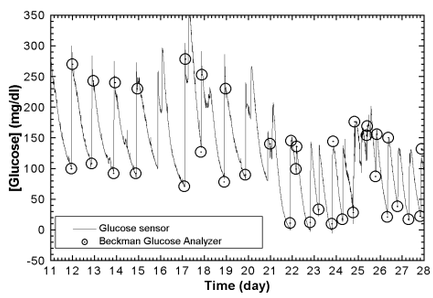

Figure 1. Plot of glucose concentration vs time in a RWPV bioreactor, where BHK-21 cells were fed once/twice a day

The glucose measurement error using this sensor as compared to Beckman Glucose Analyzer was ± 15 mg/dl in the period of 16 days. The sensor was able to continuously measure glucose for 30 days in the bioreactor cell run using two calibrations. In addition, the factors, which influence the sensor properties such as pH of the medium, flow rate and temperature were also examined and the conditions were optimized for the sensor.

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